

REMARKS

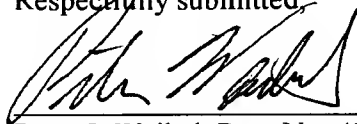
Entry of this preliminary amendment is respectfully requested.

This application is a divisional of copending application no. 09/420,347. Claims 3-6, 8-15, 17, 19-22, 25, 34, 35, 37-42 and 45-49 have been cancelled without prejudice or disclaimer. Claims 1, 2, 7, 16, 18, 23, 24, 26-33, 36, and 43-44 are amended to remove nonelected subject matter and to correct multiple dependencies. Claims 50-54 have been added. New claims 50-54 rewrite original claims 37, 41, and subject matter cancelled from pending claim 44. Claims 1, 2, 7, 16, 18, 23, 24, 26-33, 36, 43-44, and 50-54 are based on the corresponding claims as originally filed in the parent application and are directed to the subject matter of **Group V** which has not elected in the parent application. No new matter is added.

Accordingly, claims 1, 2, 7, 16, 18, 23, 24, 26-33, 36, 43-44, and 50-54 are pending and at issue in this application.

It is believed that the claims are in condition for allowance, and a determination to that effect is earnestly solicited. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,



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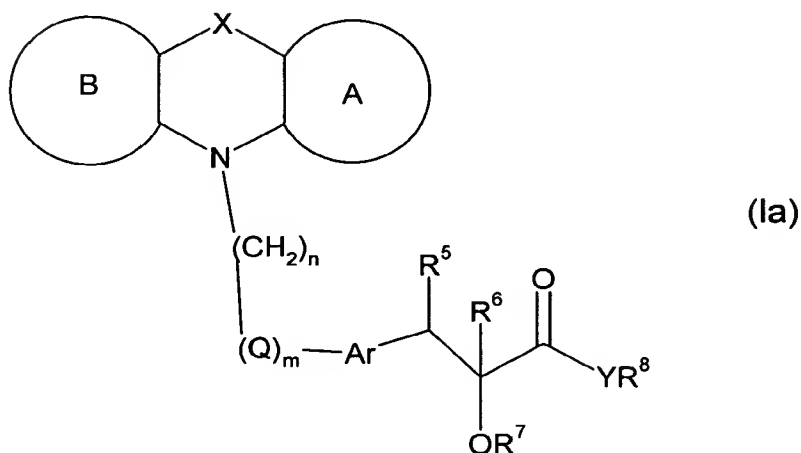


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PATENT TRADEMARK OFFICE

MARKED-UP VERSION OF THE CLAIMS SHOWING AMENDMENTS MADE

1. (Amended) A compound of formula (Ia)



wherein ring A₁ fused to the ring containing X and N₁ represents a 5-6 membered cyclic ring[,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₁₂alkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, perhalomethyl, C₁₋₆alkoxy or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

ring B₁ fused to the ring containing X and N₁ represents a 5-6 membered cyclic ring[,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl,

C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₁₂alkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, perhalomethyl, C₁₋₆alkoxy or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

X is [a valence bond, -(CHR⁹)-, -(CHR⁹)-CH₂-, -CH=CH-, -O-,] -O-(CHR⁹)-, -S-(CHR⁹)-, -(NR⁹)-CH₂-, [-(CHR⁹)-CH=CH-, -(CHR⁹)-CH₂-CH₂-, -(C=O)-, -O-CH₂-O-, -(NR⁹)-, -(NR⁹)-S(O₂)-, -CH=(CR⁹)-, -(CO)-(CHR⁹)-,] -CH₂-(SO)-, [-S-, -(SO)-, -(SO₂)-,] -CH₂-(SO₂)-, -CH₂-O-CH₂-, wherein R⁹ is hydrogen, halogen, hydroxy, nitro, cyano, formyl, C₁₋₁₂alkyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, C₁₋₆alkoxy, amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl;

Q is -O-, -S-, >SO₂, >NR¹³, wherein R¹³ is hydrogen or C₁₋₆alkyl,

Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C₁₋₆alkyl or aryl;

R⁵ represents hydrogen, hydroxy, halogen, C₁₋₁₂alkoxy, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl,

C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R⁵ forms a bond together with R⁶,

R⁶ represents hydrogen, hydroxy, halogen, C₁₋₁₂alkoxy, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, acyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R⁶ forms a bond together with R⁵,

R⁷ represents hydrogen, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, aryl, aralkyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, C₁₋₁₂alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups[:], optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

R⁸ represents hydrogen, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl groups; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

Y represents oxygen, sulphur or NR¹⁰, where R¹⁰ represents hydrogen, C₁₋₁₂alkyl, aryl, hydroxyC₁₋₁₂alkyl or aralkyl groups or when Y is NR¹⁰, R⁸ and R¹⁰ may form a 5 or 6 membered nitrogen containing ring, optionally substituted with one or more C₁₋₆alkyl;

n is an integer ranging from 1 to 4 and m is an integer ranging from 0 to 1[, provided that A or B does not represent phenyl; or a pharmaceutically acceptable salt thereof.

2. (Amended) [A] The compound according to claim 1, wherein ring A_x fused to the ring containing X and N_x represents a 5-6 membered cyclic ring[,] optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, C₁₋₇alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₇alkyl, amino, acylamino, C₁₋₇alkyl-amino, arylamino, aralkylamino, aminoC₁₋₇alkyl, C₁₋₇alkoxyC₁₋₇alkyl, aryloxyC₁₋₇alkyl, aralkoxyC₁₋₇alkyl, C₁₋₇alkylthio, thioC₁₋₇alkyl, C₁₋₇alkoxycarbonylamino,

aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

7. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1, wherein ring B₁ fused to the ring containing X and N₁ represents a 5-6 membered cyclic ring[, optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, C₁₋₇alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₇alkyl, amino, acylamino, C₁₋₇alkyl-amino, arylamino, aralkylamino, aminoC₁₋₇alkyl, C₁₋₇alkoxyC₁₋₇alkyl, aryloxyC₁₋₇alkyl, aralkoxyC₁₋₇alkyl, C₁₋₇alkylthio, thioC₁₋₇alkyl, C₁₋₇alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

16. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Q is -O- or -S-.

18. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C₁₋₆alkyl or aryl;
R⁵ represents hydrogen, hydroxy, halogen, C₁₋₇alkoxy, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl; or R⁵ forms a bond together with R⁶,
R⁶ represents hydrogen, hydroxy, halogen, C₁₋₇alkoxy, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl; or R⁶ forms a bond together with R⁵,
R⁷ represents hydrogen, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, aryl, aralkyl, C₁₋₇alkoxyC₁₋₇alkyl, C₁₋₇alkoxycarbonyl, aryloxycarbonyl, C₁₋₇alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups;

R⁸ represents hydrogen, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl;

Y represents oxygen, sulphur or NR¹⁰, where R¹⁰ represents hydrogen, C₁₋₇alkyl, hydroxyC₁₋₇alkyl;

n is an integer ranging from 2 to 3 and m is an integer ranging from 0 to 1.

23. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein A is 5 membered cyclic ring containing S.

24. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein B is 5 membered cyclic ring containing S.

26. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein n is 2.

27. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Q is -O-.

28. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein m is 1.

29. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Ar is phenylene.

[In another preferred embodiment, the present invention is concerned with compounds of formula I wherein R⁵ is H.]

30. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R⁶ is H.

31. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R⁷ is ethyl.

32. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Y is oxygen.

33. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R⁸ is H.

36. (Amended) A pharmaceutical composition comprising[,] as an active ingredient, [a] the compound according to [any one of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

43. (Amended) A method for the treatment [and/or prevention] of conditions mediated by nuclear receptors, in particular the Peroxisome Proliferator-Activated Receptors (PPAR), the method comprising administering to a subject in need thereof an effective amount of [a] the compound according to [any one of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof[, or of a composition according to anyone of the preceding claims 36-41].

44. (Amended) A method for the treatment [and/or prevention] of diabetes [and/or obesity], the method comprising administering to a subject in need thereof an effective amount of [a] the compound according to [anyone of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof[, or of a composition according to anyone of the preceding claims 36-41].